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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,365	10/20/2008	Morten Albrechtsen	ALBRECHTSEN2	2440

1444 7590 08/31/2010

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EXAMINER	
BALLARD, KIMBERLY	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
08/31/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,365	ALBRECHTSEN ET AL.	
	Examiner	Art Unit	
	Kimberly Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 June 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-12,14-32 and 35-49* is/are pending in the application.

4a) Of the above claim(s) *6-10 and 22-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,11,12,15-17,20,21,35 and 38-49* is/are rejected.

7)☒ Claim(s) *14,18,19,36 and 37* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *04/17/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I and SEQ ID NOs: 1 and 2 in the reply filed on June 14, 2010 is acknowledged. Applicants note that claims 1, 4-6, 11, 12, 14-21 and 35-49 read on the elected sequences. The examiner notes that the peptides of SEQ ID NOs: 1 and 2 are both derived from NCAM, and therefore the subject matter of claim 6 (peptides derived from cell-surface receptors) is not directed to the elected sequences. The traversal is on the ground(s) that the claims are directed to only one product (compound) claim in independent form (claim 1). The special technical feature linking the claims is the combination of structural elements, i.e., the amino acid sequence of the formula L1-A-L2-B-L3-C-L4-D-L5 and the linker X [(A)nCOOH] [(B)mCOOH]. Applicants argue that because the examiner has failed to cite prior art against claim 1, and because claim 1 is generic in form, it unifies all of the compounds it covers, as described under PCT Administrative Instructions, Annex B, paragraph (c).

Applicants also assert that claim 1 is not a Markush claim, although some elements are defined by Markush groups according to PCT Administrative Instructions, paragraph (f). As amended, claim 1 now requires the component peptide and the compound to be capable of binding to fibroblast growth factor receptor. Further, Applicants note, the component peptide have common structural elements, and dependent claim 11 has been amended to only recite those peptides that have a minimum of 3 aa positions that are identical to SEQ ID NO: 1, wherein it is noted that 69

sequences satisfy the motif of claim 1. All of the peptides are derived from a protein with an FGFR binding motif, comprise at least part of said FGFR binding motif, and thus there is an expectation of functionality. The linker too may also influence the activity of the compound, and thus contributes to the functional relationship.

Applicants' arguments have been fully considered but they are not deemed persuasive. The recited peptides set forth in claims do not appear to have a substantial structural similarity and a common utility as a whole, and therefore restriction to a single compound (in this case, two peptide sequences which comprise the claimed compound) is required. The sequences are admittedly not all derived from the same protein molecule (in this case, SEQ ID NO: 1 is derived from NCAM). While showing a small degree of homology among some of the peptide sequences, the exhibit (Exhibit 1) provided by Applicants does not show that the 69 peptides set forth in claim 11, or the peptides recited in the other claims, share a common structure, such as a binding domain. The fact that they share a minimum of 3 amino acid positions does not constitute a "significant structural element".

Moreover, the peptides do not appear to share a common utility. For example, because they are derived from diverse proteins having different and unique biological activities through their interactions with different FGF receptors, the peptides derived from these proteins would similarly not be expected to bind the same FGF receptors nor produce the same biological responses.

Further, the amended claims have been reconsidered. PCT Rule 13.2 defines "special technical features" as "those technical features that define a contribution which

each of the claimed inventions, considered as a whole, makes over the prior art." Claim 1 is drawn to a compound comprising two individual peptide sequences, however, the prior art teach the instantly claimed compound. For example, WO 03/016351 by Kiselyov et al. (listed on IDS) teaches a peptide (SEQ ID NO: 1, p. 17, line 19) that is identical to the instant SEQ ID NO: 1. Kiselyov also teaches that this NCAM derived peptide, which is capable of binding with an FGF receptor (see p. 23, lines 4-7), may be comprised in a compound that is a dimer (p. 25, lines 9-10). The dimer may comprise to identical monomers, or two monomers different from each other (p. 25, lines 23-26). Kiselyov does not teach the linkers recited in claim 1. However, WO 00/18791 by Holm discloses a peptide linker of the formula X [(A)nCOOH] [(B)mCOOH] consistent with the linker formula recited in present claim 1 (see pp. 15-17). Holm discloses an assembly method comprising use of the aforementioned formula as a core molecule (i.e., a linker for a dimer molecule), and teaches that this method is advantageous to previously known methods because it overcomes the problem of racemisation (i.e., instead of obtaining a single product, a mixture of diastereomers are obtained). Therefore, it would have been obvious to use the core molecule of X [(A)nCOOH] [(B)mCOOH] as a peptide linker (and disclosed assembly method), as taught by Holm, in the peptide dimer as taught by Kiselyov. Thus, the technical feature linking the different peptide sequences does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

Finally, with respect to the species election regarding the different diseases or conditions, Applicants elect Alzheimer's disease with traverse. The examiner regrets

that the species election was not clearer so as to alleviate any unnecessary confusion. The species election for diseases/conditions was meant only with respect to group II, and therefore, does not pertain to elected group I.

2. Claims 6-10 and 22-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions or sequences, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on June 14, 2010.

3. Claims **1, 4, 5, 11, 12, 14-21** and **35-49**, to the extent the read upon the elected sequences of SEQ ID NOs: 1 and 2, are under examination in the current office action.

Information Disclosure Statement

4. The information disclosure statement (IDS) filed April 17, 2008 has been considered and the references therein are of record. However, 37 CFR 1.98(b)(5) states: "Each publication listed in an information disclosure statement must be identified by publisher, author (if any), title, relevant pages of the publication, date, and place of publication. " Reference #33 fails to list a date. It is also noted that the actual article has a different title and author from the reference listing, wherein it is presumed the reference is an article from within the book/journal listed as Reference #33. Therefore, the reference has been lined through.

Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Priority

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

6. Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The

disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

7. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. §1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of C.F.R. §§ 1.821-1.825. The disclosure contains sequences that require reference to particular sequence identifier numbers (SEQ ID NO:), such as on page 3, line 9. Additionally, at page 11, line 31, the specification recites the peptide sequence EVYVVAENAAGKSKA (SEQ ID NO: 147), but there is no SEQ ID NO: 147 in the originally filed sequence listing. In case these sequences are not in the originally filed sequence listing, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", and amendment directing the entry of that paper copy into the specification, and where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). Applicant is advised to review the entire text of the instant specification for compliance with sequence rules.

Claim Objections

8. Claim 20 is objected to because of the following informalities: the claim recites an acronym that is not spelled out in its first use in the claims (i.e., LPA). It would be

remedial to amend the claim language in claim 20 such that the acronym is clearly defined. Appropriate correction is required.

9. Claims 40-42, 46 and 47 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 40-42 recite the compound of claim 1, wherein at least one peptide sequence comprises a sequence having at least 50%, 60%, or 90% positive amino acid matches with SEQ ID NO: 1. The specification defines a positive amino acid match at p. 26 as "an identity or similarity defined by physical and/or chemical properties of the amino acids having the same position in two compared sequences". Such sequences encompass variants of the claimed peptide sequences which comprise the compound of claim 1. The claims do not state whether this variant peptide sequence is *the* "at least one" sequence of claim 1 (i.e., the peptide sequence according to formula (I)) or whether it is the "other" peptide sequence, and therefore it could reasonably be either peptide sequence of the dimer compound. If this new variant peptide sequence is meant to be the peptide sequence of formula (I) of claim 1, however, it would fail to further limit the compound because such a sequence would expand the scope of the peptide of formula (I).

Similarly, claims 46 and 47 recite the compound of claim 1, wherein at least one of the individual peptide sequences comprises the sequence (D/E/N/Q)- 3 amino acids- (R/K/H) (claim 46), or N- 3 amino acids- K (claim 47). In each case, only 2 positions of

the amino acid sequence are defined. Again, should this peptide sequence be *the* defined peptide sequence of claim 1 according to formula I, then claims 46 and 47 effectively *expand* the scope of the claimed peptide sequence.

Applicant should note the "Infringement Test" for dependent claims in MPEP 608.01(n). The test for a proper dependent claim is whether the dependent claim includes every limitation of the parent claim. A proper dependent claim shall not conceivably be infringed by anything which would not also infringe the basic claim. In the instant case, the variant sequence having at least some percentage positive amino acid matches with SEQ ID NO: 1 as in claims 40-42, and the peptide sequence according to the formulas of claims 46 and 47, could be infringed without infringing the claim from which it depends, i.e., the peptide sequence of formula I. Therefore, the claims are improperly dependent.

Claim Rejections - 35 USC § 112, second paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 4, 5, 15, 16 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 4 and 5 each recite the phrase "selected from the group consisting of" and then list items in the group in an open format. For example, claim 4 recites "...heparan sulfate proteoglycans, ***and*** metalloproteases, extracellular matrix molecules

or growth factors." And claim 5 recites "...Intercellular Cell Adhesion Molecule-5...***or*** Galactose binding lectin-12..., ***and*** Galactose binding lectin-4..." MPEP 2173.05(h)(I), Markush Groups, states "[a]lternative expressions are permitted if they present no uncertainty or ambiguity with respect to the question of scope or clarity of the claims." However, in each of the present claims the scope of the encompassed groups is indefinite, because it is unclear what the groups actually consist of, that is, the items in the group are recited in the alternative "or". Therefore the metes and bounds of the claims cannot be determined.

13. Claims 15 and 16 recite the limitation "said group of amino acid sequences" in line 5 of claim 15 and lines 4-5 of claim 16. There is insufficient antecedent basis for this limitation in the claims.

14. Claim 49 recites the sequence AEN - 2 amino acids - GK (SEQ ID NO: 147). First, as Applicant has correctly noted in their response filed June 14, 2010, the sequence listing does not list SEQ ID NO: 147, as there are only 146 sequences currently in the sequence listing. However, as noted above, the instant specification already recites a SEQ ID NO: 147 at page 11, line 31, which is given as EVYVVAENAAGKSKA. Even though the "new" sequence of AEN - 2 amino acids - GK is comprised by the "old" sequence EVYVVAENAAGKSKA, the new sequence encompasses a much broader scope than the old sequence. Therefore, it is unclear

whether the SEQ ID NO: 147 of claim 49 is meant to be the "new" sequence of the new claim or the "old" sequence of the specification as filed.

Claim Rejections - 35 USC § 112, first paragraph

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1, 4, 5, 15, 16, 20, 21, 38-42, 44-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a compound comprising two individual peptide sequences, wherein at least one of the two individual peptide sequences comprises an amino acid sequence of the formula (I): L1-A-L2-B-L3-C-L4-D-L5, wherein said peptide sequence and said compound are capable of binding to an FGF receptor. The claims also recite that the peptide sequence has at least 50%, 60%, or 90% positive amino acid matches with SEQ ID NO: 1, the compound comprises a sequence at least 90% identical to SEQ ID NO: 1, or at least one of the peptide sequences comprises the sequence X1-X2-X3-X4-X5-X6-X7-X8, (D/E/N/Q)- 3 aa - (R/K/H), or (A/G) – (D/E/N/Q) –

(2 amino acids) – (A/G) – (R/K/H). The claimed invention thus encompasses compounds which are comprised of a very broad genus of peptide sequences.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Applicants are directed to the recently-published guidelines on interpretation of the written description requirement, available on the internet at: http://www.uspto.gov/web/menu/written.pdf . See in particular Examples 9 and 10, drawn to protein variants including those with recited functions.

The recitation of a compound comprising a generic formula and capable of binding to FGFRs represents a partial structure and a functional characteristic, respectively. While at least one of the peptides of the dimer compound has the formula L1-A-L2-B-L3-C-L4-D-L5, it is noted that there is substantially variable within this sequence formula, particularly since any of A, B, C, or D can each individually be any of 15 different amino acids, and any of L1, L2, L3 or L4 may be absent (a chemical bond) or have up to 5 amino acid residues. In considering the size of the genus, it is noted that if one simply considered naturally occurring amino acids at certain positions, and depending on what is selected by each of A, B, and C, formula I (claim 1) is such that A has 15 possibilities, B would have 9 to 13 possibilities, C would have 6 to 11 possibilities, and D would have 2 to 6 possibilities. This means that for positions A-D,

there can be over 12,000 possibilities for these positions. For the L positions (L1-L5; i.e., an amino acid sequence having 0 to 5 amino acid residues), each position has at least 20 different possibilities, which means there are at least 3.2×10^6 possibilities (20x20x20x20x20) for the L positions. A *conservative* estimate for the number of possible peptide sequences that could be made according to the claimed formula I would therefore encompass over 3.8×10^{10} different sequences for the "at least one" peptide sequence, and multiples more so for the claimed dimer compound. In other words, the peptide sequence can vary substantially within the given claimed recitations.

The instant specification does not provide sufficient guidance as to which of the amino acid residues within the claimed peptide sequences fan be varied while still retaining the capacity to bind FGF receptors, and presumably, to elicit biological activities such as neurite outgrowth. There is no specific disclosed correlation between structure and function. While Applicant has disclosed a formula comprising particular amino acid residues, as noted above, there is the potential for substantial variability within the bounds of this formula such that one of skill in the art would not immediately recognize peptides comprising this formula other than those that are specifically identified by the specification. The specification provides 3 examples (SEQ ID NOs: 1, 2 and 5) of biologically active monomer and/or dimer peptides capable of binding FGFR1. In addition, the specification provides 146 sequences listed in 12 different groups that are reported to comprise at least one of the claimed structural motifs, and Applicants' response filed June 14, 2010 notes that 69 sequences satisfy the motif of claim 1. In particular, Applicants note that SEQ ID NOs: 2-8, 11-73, 97-99 and 114-145

have a minimum of three amino acid positions with SEQ ID NO: 1. However, in view of the extensive variably presented by formula 1, the lack of identification of any particular portion or residue of the peptide that must be conserved for FGFR binding, and in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus nor guidance as to which of they myriad of molecules encompassed by the claimed compound would meet the limitations of the claims.

There is substantial variability within the genus. Since there are a variety of compound possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NOs: 1, 2 and 5, the skilled artisan cannot envision the detailed chemical structure of the encompassed claimed compounds (if any) which have the activity of binding FGFRs without further testing, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of identification. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method

of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483 (BPAI 1993). In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only compounds comprising the peptide sequences of SEQ ID NO: 1, 2 or 5, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicants are reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

17. Claims 45-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The claims recite peptide sequence motifs which are not explicitly described in the present specification as filed. The new claim limitations appear to be based upon the response filed June 14, 2010 at pages 20-21, which compares the motif requirements for the elected sequences of SEQ ID NOs: 1 and 2. While the elected

sequences of SEQ ID NOs: 1 and 2 may indeed follow the rules of the recited motifs, the scope of the encompassed sequences defined by the motifs is far broader than the actual peptide sequences of SEQ ID NOs: 1 and 2, and as noted above, in certain instances is broader than the peptide sequence comprising formula I of claim 1. These peptide sequence motifs thus represent a genus of peptide sequences for which Applicant has highlighted only two species, SEQ ID NOs: 1 and 2, within the genus. And even were additional disclosed sequences to fall within the scope of the peptide motifs, the fact remains that these motifs were not explicitly recognized or stated at the time the instant application was filed. There may well be other peptide sequence motifs that could be recognized based upon the alignment of two other peptides of the 146 disclosed sequences, but which similarly have not yet been recognized. The motifs allow for a subgenus of peptide sequences not originally envisioned by the disclosure as filed, and therefore they constitute new matter.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1, 4, 5, 11, 12, 15-17, 20, 21, 35 and 38-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 03/016351 by Kiselyov et al. (published 27 February 2003; reference #4 on Applicants' IDS) in view of WO 00/18791 by Holm (published 6 April 2000; reference #7 on IDS).

Kiselyov et al. disclose a compound capable of binding the Fibroblast Growth Factor (FGF) receptor, including FGFR1 (see p. 23, lines 4-7), wherein the compound comprises at least one peptide which comprises the formula L1-A-L2-B-L3-C-L4-D-L5, wherein one of A, B, C, or D is selected from a basic amino acid residue, one of A, B, C, or D is selected from a hydrophobic amino acid residue, one of A, B, C, or D is selected from an acidic amino acid residue, one of A, B, C, or D is glycine, and L1, L2, L3, L4 and L5 may be selected from a chemical bond or an amino acid sequence having n

amino acid residues, wherein n is an integer of from 0 to 5 (see p. 15, lines 1-12). Such teachings are on point to formula I of claim 1. Kiselyov also discloses the more precise formulas of AENQ-L4-G, wherein L4 may be a chemical bond or 0 to 5 amino acids (p. 15, lines 25-32), as well as the sequence A-E-N-Q-X-X-K, wherein each X may be any amino acid or it may be individually selected from gln (Q), ala (A), gly (G) and/or asn (N) (see p. 15, lines 34-39). These disclosed peptide sequences thus provide for recited limitations of instant claims 45-49.

Kiselyov further discloses the peptide sequence of EVYVVAENQQGKSKA (SEQ ID NO: 1; see p. 17, line 19), which is identical to the instant peptide sequence of SEQ ID NO: 1, and which is notably derived from NCAM. Kiselyov teaches that the compound of the invention may be a dimer, wherein the individual monomers of the dimer may be heterologous, i.e., different from one another, or homologous, i.e., identical to one another. Thus, a dimer compound comprising either one or two copies of Kiselyov's SEQ ID NO: 1 would meet the limitations of claim 15 (different peptide sequences), 16 (identical peptide sequences), 17 (identical sequences that each consist of SEQ ID NO: 1), 35 (identical fragments that each comprise SEQ ID NO: 1), 38 (both peptides satisfy formula I), 39 (comprises at least 9 consecutive amino acids of SEQ ID NO: 1), 40-42 and 44 (comprises a sequence at least some percent matching/identical with SEQ ID NO: 1), 43 (consists of SEQ ID NO: 1), and 45-49 (comprises the recited peptide sequence motifs). Kiselyov also discloses pharmaceutical compositions comprising the compound, wherein the compositions are preferably formulated as dimers (see p. 26, line 6), which address present claim 21.

Although Kiselyov discloses dimer compounds, the difference between the teachings of Kiselyov and the present invention is that the prior art reference does not teach a linker of the formula (II), as in claim 1.

Holm teaches a ligand presenting assembly (LPA) method for preparing dimeric and multimeric compounds which is based on the assembly of two peptide chains attached to a solid phase by means of achiral dicarboxylic, tricarboxylic or tetracarboxylic acids (see abstract and p. 14, lines 23-26). Holm teaches that by using achiral compounds, racemisation problems are avoided, thus allowing rigorous activation conditions for difficult reactions (p. 14, lines 26-28). Suitable achiral di-, tri- and tetracarboxylic acids to be used are disclosed to have the formula: $X[(A)_nCOOH][(B)_mCOOH]$ (see p. 15, lines 8-11), wherein the definitions for X, A, B, n and m are given at pp. 15-17 and notably include limitations consistent with those of instant claim 1.

With respect to claim 20, it is noted that process by which the compound is obtained does not in fact change the claimed product, which is a compound comprising two individual peptide sequences and a linker. See MPEP § 2113, which states that:

> [E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

Regardless, Holm discloses a method at pp. 9-10 comprising the steps of:

(a) providing by solid phase synthesis or fragment coupling ligand(s) comprising the desired sequence(s), the ligand(s) being attached to a solid phase,

(b) if necessary, deprotecting any N-terminal amino groups while the ligand(s) are still attached to the solid phase,

(c) reacting the ligand(s) having unprotected N-terminal amino groups with an achiral di-, tri- or tetracarboxylic acid so as to provide a construct having a ring structure, and

(d) cleaving the construct from the solid phase so as to provide an LPA comprising ligand(s) having free C-terminal groups.

Such a method is identical to that which is presently recited in claim 20. Holm teaches that the method is easily performed, and with some additional steps to step (c), may be used to assemble desired sequences which are identical or different sequences (see paragraph spanning pp. 10-11). Therefore, LPAs are suitable and very flexible systems for polyfunctional constructs, and furthermore, products of high purity are obtained (p. 11, lines 3-5).

It would have been obvious to one of ordinary skill in art at the time the invention was filed to use the LPA method disclosed by Holm, which would include the use of achiral di-, tri- and tetracarboxylic acids of the formula X $[(A)_nCOOH][(B)_mCOOH]$ as linker molecules, in the production of a dimer compound as taught by Kiselyov, and arrive at the presently claimed invention. This is because the artisan has good reason to pursue the known options within his or her technical grasp to obtain predictable results. Such would amount to the use of a known technique (i.e., Holm's LPA method)

to improve similar products (i.e., Kiselyov's dimeric peptide compounds) in the same way. Particularly in view of the noted benefits attributed to Holm's LPA method of preparing polyfunctional constructs (ease of preparation, the ability to include non-identical sequences, high purity of resulting compound), the artisan would be motivated to use the achiral linker molecules and would also reasonably expect success in the preparation of the dimeric compounds. Accordingly, the combined teachings of the references render obvious the presently recited invention of claims 1, 4, 5, 11, 12, 15-17, 20, 21, 35 and 38-49.

Conclusion

20. Claims 1, 4, 5, 11, 12, 15-17, 20, 21, 35 and 38-49 are rejected. Claims 14, 18, 19, 36 and 37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Ballard whose telephone number is 571-272-2150. The examiner can normally be reached on Monday-Friday 8:30 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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